510k Summary

This 510k Summary information is supplied in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is K131284

Date: November 14, 2013

Submitted by: Wallac Oy, a subsidiary of PerkinElmer Inc.
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NOV 14 2013

Submission Contact Person:
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Trade Name: GSP Neonatal Biotinidase kit

Common Name: Biotinidase test system
Regulation: 21 CFR 862.1118

Classification Name: Biotinidase test system

Classification: II

Panel: 75 Clinical Chemistry

Product Code: NAK

Predicate device: PerkinElmer Neonatal Biotinidase kit [K090123]

Device Description:

The GSP Neonatal Biotinidase kit contains sufficient reagents to perform 1152 assays. The GSP Neonatal Biotinidase test system measures biotinidase activity, combining an enzyme reaction with a solid phase time-resolved immunofluorescence assay. The GSP Neonatal Biotinidase assay is based on the ability of the biotinidase enzyme to cleave the amide bond in Eu-labeled biotin. The enzyme reaction is stopped by addition of streptavidin which has high affinity for biotin (either Eu-labeled or free biotin). The streptavidin-biotin complexes are captured by the solid phase monoclonal antibody directed against streptavidin. DELFIA Inducer dissociates the molecules into the solution where the europium fluorescence is measured. The measured fluorescence is inversely proportional to the biotinidase activity of the sample.

The kit contains the following components:

Calibrators have been prepared from human whole blood using ProClin 300 as preservative. The biotinidase calibrators' activities range from 10 U/dl to 325 U/dL. As no internationally accepted reference material or a reference method for the determination of biotinidase activity is available, the calibrators have been calibrated against in-house primary calibrators (dried blood spots, stored at -80 to -60°C) prepared using adult human blood (endogenous biotinidase activity in serum) and washed red blood cells as blood matrices.

Controls have been prepared from human whole blood using ProClin 300 as preservative. The low control is approximately 40.0 U/dL and the high control approximately 160 U/dL.

All human source materials used in the preparation of kit components were tested and found to be negative for hepatitis B surface antigen, anti-hepatitis C and anti-HIV 1 and 2 derivatives by FDA approved methods.

Biotinidase Substrate Reagent – 3 ready-to-use vials, 2.8 ml each
Biotinidase SA Reagent – 3 ready-to-use vials, 2.8 ml each
Assay Buffer – 3 bottles, 120 ml each
Anti-SA Microtitration Strips – 12 plates

Intended Use:

The GSP Neonatal Biotinidase kit is intended for the quantitative in vitro determination of human biotinidase activity in blood specimens dried on filter paper as an aid in screening newborns for biotinidase deficiency using the GSP® instrument.

Comparison Chart:

Comparison of the GSP Neonatal Biotinidase kit (proposed device) with its predicate:

Characteristics	Proposed Device – GSP Neonatal Biotinidase kit	Predicate (K090123)
Intended Use/Indications for Use	The GSP Neonatal Biotinidase kit is intended for the quantitative *in vitro* determination of human biotinidase activity in blood specimens dried on filter paper as an aid in screening newborns for biotinidase deficiency using the GSP® instrument.	This kit is intended for the semi-quantitative determination of biotinidase in blood specimen dried on filter paper as an aid in screening newborns for biotinidase deficiency.
Specimen Type	Dried blood spot	Same
Assay Technology	Enzymatic assay	Same
Kit Content	Calibrators, enzymatic reagents, kit controls (additionally includes mocrotiter plates and bar code labels for use with the GSP instrument)	Calibrators, enzymatic reagents, kit controls (additionally includes mocrotiter plates)

Interpretation of Results	Calibration Curve	Same
Test Principle	Combines an enzyme reaction with a solid phase time-resolved immunofluorescence assay. Biotinidase in the sample cleaves the amide bond in the Eu-labeled biotin substrate. The end product is captured using Streptavidin and Anti-streptavidin coated plate. DELFIA® Inducer dissociates the molecules into the solution where the europium fluorescence is measured	1-step enzymatic assay were the biotinidase in the sample cleaves the substrate biotin 6- aminoquinoline generating a fluorescent 6-aminoquinoline product
Instrument Platform	GSP instrument, automated (K090846)	Fluorometer, manual
Detection Method	Time-resolved fluorescence	Fluorometer with excitation central wavelength of 355 nm and the emission central wavelength of 460 nm
Screening Outcome	Normal and Deficient	Same
Measuring Unit	U/dL	U
Calibrator Matrix	Dried blood spots prepared from human whole blood	Dried blood spots prepared from porcine blood
Calibrator Levels	Six levels, ready to use 10 U/dL 25 U/dL 50 U/dL 100 U/dL 175 U/dL 325 U/dL	Six levels, ready to use 10 U 30 U 130 U 180 U 250 U 350 U
Measuring Range	14.8 U/dL - 325 U/dL	16 U – 350 U
Lower Limits of Measure	LoB = 9.5 U/dl LoD = 14.8 U/dl LoQ = 14.8 U/dl	LoB = 12 U LoD = 16 U

Summary of Non-Clinical Studies:

The variation of the GSP Neonatal Biotinidase assay was determined using dried blood spot samples, 3 kit lots, and 3 GSP instruments. The study was performed in 27 runs over 20 days, each run consisting of 2 plates with 4 replicates per sample. Total number of measurements was 216 per sample. Total variation ranged from 7.5 to 12.7 %CV.

The limit of blank, detection and quantity were determined according to the CLSI guideline EP17-A.The Limit of Blank (LoB) for GSP Neonatal Biotinidase kit is 9.5 U/dL, defined as the 95th percentile of a distribution of blank samples (n=150). The Limit of Detection (LoD) is 14.8

U/dL based on 360 determinations of five low level samples. The Limit of Quantitation (LoQ) is 14.8 U/dL, defined as the lowest activity with a total CV equal or less than 20%.

Linearity was determined in accordance with CLSI document EP6-A. For GSP Neonatal Biotinidase, the method has been demonstrated to be linear throughout the measuring range (from 14.8 U/dL to 325 U/dL). Recovery cannot be determined as biotinidase is not commercially available in pure form.

Ampicillin (1.4 mg/dL and above), sulfisoxazole (7.5 mg/dL and above) at low biotinidase activity levels (35 U/dL) and ampicillin (2.8 mg/dL) at high biotinidase activity levels (150 U/dL) were found to interfere with this test by increasing measured biotinidase activity by 19.9%, 32.1% and 15.6%, respectively. Elevated ampicillin and sulfisoxazole levels near the biotinidase cut-off did not exhibit a significant effect (<15%).

Glutathione levels above normal (> 30 mg/dL) can interfere with this test by increasing biotinidase activity by 16.1% or more. This could result in the misclassification of a patient with a biotinidase result near the cut-off value as 'normal' when in fact the patient should be classified as 'deficient'. A patient with known or clinically suspected elevated blood glutathione concentration (>30 mg/dL)should be screened with an alternative method and confirmed according to local requirements for follow-up testing.

Unconjugated bilirubin (10 mg/dL) added to whole blood at low biotinidase activity levels (35 U/dL) were found to interfere with this test by increasing measured biotinidase activity by 18.7%. Elevated unconjugated bilirubin level (20 mg/dL) near the biotinidase cut-off did not exhibit a significant effect (<15%).

Conjugated bilirubin (2.5 mg/dL and above) and triglyceride (250 mg/dL and above) added to whole blood were found to interfere with this test by decreasing measured biotinidase activity by 26.0% and 15.7%, respectively. Elevated conjugated bilirubin (2.5 mg/dL and above) and triglyceride levels (250 mg/dL and above)may cause a false positive screening result for a specimen with measured biotinidase activity near the cut-off.

The following substances were found not to interfere at concentration indicated; adrenocorticotropic hormone (15 ng/dL), ascorbic acid (3 mg/dL), biotin (500 ng/dL), Gammaglobulin (3 g/dL), gentamicin sulphate (0.5 mg/dL), hemoglobin (1.6 g/dL), human serum albumin (6 g/dL), kanamycin sulphate (3 mg/dL), penicillin G (25 mg/dL), phenytoin (2.5 mg/dL), phenobarbital (5.5 mg/dL), sulfmethoxazole (20 mg/dL), trimethoprim (2 mg/dL), valporic acid (19 mg/dL), and vitamin K1 (0.1 mg/dL).

Summary of Clinical Studies:

The 3307-001U GSP Neonatal Biotinidase kit was compared to the 3018-0010/3018-001B Neonatal Biotinidase kit in a routine screening laboratory by measuring the biotinidase activity in a total of 2008 specimens. These included routine newborn screening specimens (n = 1988) and retrospective confirmed biotinidase deficiency specimens (n = 20).

The results for the screening performance data based on the predicate's cut-off of 30% of mean + 2SD manual Neonatal Biotinidase method classified all 20 biotinidase deficient specimen as screening positive. The GSP Neonatal Biotinidase method used cut-off based on 0.5th percentile and classified 19 specimens as screening positive and 1 specimen as screening negative based on the initial test result. In multiple (4) repeat tests this specimen was positive at all cut-offs. Duplicate punches in the same microtiter well (due to static electricity) were concluded to be the potential cause for the initial false negative result. The results are shown below.

GSP result	Predicate result	Total	Positive	Normal
+	+	23	19	4
+	-	6	0	6
-	+	2	1*	1
-	-	1977	0	1977
Total		2008	20	1988

* One retrospective confirmed biotinidase deficiency specimen that initially tested as negative; tested as positive in 4 repeat tests.

The following table illustrates the screening performance of the GSP Neonatal Biotinidase test system in comparison to the predicate device using the 0.5th percentile cutoff based on population distribution and using the 30% of mean + 2SD cut-off for manual Neonatal Biotinidase method. The percent agreement calculations have been performed for the comparison.

		3018-0010/3018-001B 30% of mean + 2SD		
		Screen positive ≤ 67.6 U	Screen negative > 67.6 U	Total
GSP 3307-001U 0.5th percentile	Screen positive ≤ 74.6 U/dL	23*	6	29
	Screen negative > 74.6 U/dL	2**	1977	1979
	Total	25	1983	2008

* Includes 19 retrospective confirmed biotinidase deficiency specimens.
** One retrospective confirmed biotinidase deficiency specimen that initially tested as negative; tested as positive in 4 repeat tests

Overall percent agreement = 99. 6% (CI 99.2% - 99.8%)
Positive percent agreement = 92.0% (CI 74.0% - 99.0%)
Negative percent agreement = 99.7% (CI 99.3% - 99.9%)

Substantial Equivalency:

The proposed device and predicate device utilize similar enzymatic pathway and design which is shown to produce equivalent screening performance in a clinical setting. Both devices are intended for the quantitative in vitro determination of human biotinidase activity in blood specimens dried on filter paper as an aid in screening newborns for biotinidase deficiency.

Conclusion:

The GSP Neonatal Biotinidase test system demonstrates analytical and screening performance that supports its substantial equivalency with the predicate device, the Neonatal Biotinidase test system (K090123).

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – W066-G609
Silver Spring, MD 20993-0002

November 14, 2013

Wallac Oy, a subsidiary of PerkinElmer Inc.
Ms. Jeanette Schier-Pugsley
Director, Regulatory and Clinical Affairs
940 Winter Street
WALTHAM MA 02451

Re: K131284
Trade/Device Name: GSP Neonatal Biotinidase Kit
Regulation Number: 21 CFR 862.1118
Regulation Name: Biotinidase test system
Regulatory Class: II
Product Code: NAK
Dated: October 03, 2013
Received: October 04, 2013

Dear Ms. Schier-Pugsley:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Carol C. Benson -S for

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
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Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*

K131284

Device Name

GSP Neonatal Biotinidase Kit

Indications for Use *(Describe)*

The GSP Neonatal Biotinidase kit is intended for the quantitative in vitro determination of human biotinidase activity in blood specimens dried on filter paper as an aid in screening newborns for biotinidase deficiency using the GSP instrument.

Type of Use *(Select one or both, as applicable)*

[X] Prescription Use (Part 21 CFR 801 Subpart D) [ ] Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Yung W. Chan -S